```
=> e smith daniel j/au
E1            8     SMITH DANIEL H/AU
E2            2     SMITH DANIEL I/AU
E3          301 --> SMITH DANIEL J/AU
E4            1     SMITH DANIEL JAMES/AU
E5            1     SMITH DANIEL JOHANNES/AU
E6           23     SMITH DANIEL JOHN/AU
E7            2     SMITH DANIEL JORDAN/AU
E8            4     SMITH DANIEL JOSEPH/AU
E9           13     SMITH DANIEL K/AU
E10           5     SMITH DANIEL KEITH/AU
E11           4     SMITH DANIEL L/AU
E12           3     SMITH DANIEL L JR/AU

=> s e3-e8 and (glucan or glucosyltransferase?)
L1           79 ("SMITH DANIEL J"/AU OR "SMITH DANIEL JAMES"/AU OR "SMITH DANIEL
                JOHANNES"/AU OR "SMITH DANIEL JOHN"/AU OR "SMITH DANIEL JORDAN"
               /AU OR "SMITH DANIEL JOSEPH"/AU) AND (GLUCAN OR GLUCOSYLTRANSFER
               ASE?)

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2            48 DUP REM L1 (31 DUPLICATES REMOVED)

=> s l2 and ((GbpB)or(glucan binding protein B))
L3             8 L2 AND ((GBPB) OR(GLUCAN BINDING PROTEIN B))

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 8 ANSWERS - CONTINUE? Y/(N):y


L3   ANSWER 1 OF 8  BIOSIS  COPYRIGHT (c) 2006 The Thomson Corporation  on STN
AN   2005:498381  BIOSIS
DN   PREV200510279091
TI   Characterization of salivary immunoglobulin A responses in children
     heavily exposed to the oral bacterium Streptococcus mutans: Influence of
     specific antigen recognition in infection.
AU   Nogueira, Ruchele D.; Alves, Alessandra C.; Napimoga, Marcelo H.;
     Smith, Daniel J.; Mattos-Graner, Renata O. [Reprint Author]
CS   UNICAMP, Fac Odontol Piracicaba, Dept Microbiol and Imunol, Piracicaba Sch
     Dent, Av Limeira 901, BR-13414903 Sao Paulo, Brazil
     rmgraner@fop.unicamp.br
SO   Infection and Immunity, (SEP 2005) Vol. 73, No. 9, pp. 5675-5684.
     CODEN: INFIBR. ISSN: 0019-9567.
DT   Article
LA   English
ED   Entered STN: 16 Nov 2005
     Last Updated on STN: 16 Nov 2005
AB   The initial infection of children by Streptococcus mutans, the main
     pathogen of dental caries, depends on the ability of S. mutans to adhere
     and accumulate on tooth surfaces.  These processes involve the adhesin
     antigen I/II (AgI/II), glucosyltransferases (GTF) and
     glucan-binding protein B (
     GbpB), each a target for anticaries vaccines.  The salivary
     immunoglobulin A (IgA) antibody responses to S. mulans antigens (Ags) were
     characterized in 21 pairs of 5- to 13-month-old children.  Pairs were
     constructed with one early S. mutans-infected and one noninfected child
     matched by age, racial background, number of teeth, and salivary levels of
     IgA.  Specific salivary IgA antibody response and S. mutans infection
     levels were then measured during a I-year follow-up.  Robust responses to
     S. mutans were detected from 6 months of age.  Salivary IgA antibody to
     AgI/II and GTF was commonly detected in salivas of all 42 children.
     However, GbpB-specific IgA antibody was seldom detected in the
     subset of infected children (38.1% at baseline).  In contrast, most of the
     subset of noninfected children (76.2%) showed GbpB-reactive IgA
     antibody during the same period.  Frequencies of GbpB responses
     increased with age, but differences in intensities of GbpB-IgA
     antibody reactions were sustained between the subsets.  At baseline,
     GbpB-reactive IgA antibody accounted for at least half of the
```

total salivary IgA S. mutans-reactive antibody in 33.3 and 9.5% of noninfected and infected children, respectively. This study provides evidence that a robust natural response to S. mutans Ags can be achieved by 1 year of age and that IgA antibody specificities may be critical in modulating initial S. mutans infection.

L3 ANSWER 2 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2005:278296 BIOSIS
DN PREV200510068959
TI Immunological and protective effects of diepitopic subunit dental caries vaccines.
AU **Smith, Daniel J.** [Reprint Author]; King, William F.; Rivero, Joy; Taubman, Martin A.
CS Forsyth Inst, Dept Immunol, 140 Fenway, Boston, MA 02115 USA
dsmith@forsyth.org
SO Infection and Immunity, (MAY 2005) Vol. 73, No. 5, pp. 2797-2804.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 27 Jul 2005
Last Updated on STN: 27 Jul 2005
AB As a prelude to development of broader-spectrum vaccines for dental caries, we explored the immune potential of constructs combining epitopes from mutans streptococcal **glucosyltransferases** (GTF) and **glucan binding protein B** (**GbpB**). Two diepitopic peptide constructs were synthesized in a multiple antigenic peptide (MAP) format. Both constructs contained SYI, a 20-mer **GbpB** peptide that included a sequence having major histocompatibility complex class 11 binding characteristics. One diepitopic construct (SYI-CAT) also contained a 22-mer sequence from the catalytic domain of GTF. Another diepitopic construct (SYI-GLU) contained a 22-mer sequence from the **glucan** binding domain of GTF. To assess the ability of each construct to induce antibody reactive with **GbpB** and GTF native proteins, rats were injected subcutaneously with SYI-CAT, SYI-GLU, or the constituent monoepitopic constructs. Only the SYI-CAT construct induced significant levels of serum immunoglobulin G (IgG) and IgA antibody to both pathogenesis-associated proteins. Also, immunization with SYI-CAT significantly ($P < 0.001$) enhanced the antibody response to the CAT peptide. Experiments then compared experimental dental caries after immunization with SYI-CAT, SYI, or CAT MAP constructs, followed by infection with Streptococcus mutans strain SJr. Dental caries were lower in each peptide-immunized group than in the sham-injected group. The level of protection after SYI-CAT immunization was similar to that after immunization with constituent MAP constructs. In another experiment, rats were infected with Streptococcus sobrinus strain 6715 under an identical protocol. Significant protection was observed on buccal surfaces in both SYI-CAT and CAT construct-immunized, but not in the SYI construct-immunized, groups. Thus, addition of the **GbpB** -derived SYI peptide to the GTF-derived CAT peptide construct not only enhanced the immunological response to CAT and GTF epitopes, but also extended the protective effect of the construct to include both S. mutans and S. sobrinus.

L3 ANSWER 3 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2003:172182 BIOSIS
DN PREV200300172182
TI Immunogenicity and protective immunity induced by synthetic peptides associated with putative immunodominant regions of Streptococcus mutans **glucan-binding protein B**.
AU **Smith, Daniel J.** [Reprint Author]; King, William F.; Barnes, Leigh A.; Peacock, Zachary; Taubman, Martin A.
CS Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA, 02115, USA
dsmith@forsyth.org
SO Infection and Immunity, (March 2003) Vol. 71, No. 3, pp. 1179-1184. print.
ISSN: 0019-9567 (ISSN print).
DT Article
LA English
ED Entered STN: 2 Apr 2003

Last Updated on STN: 2 Apr 2003

AB **Glucan-binding protein B** (**GbpB**) from Streptococcus mutans has been shown to induce protective immunity to dental caries in experimental models. Having recently sequenced the **gbpB** gene, our objective in this study was to identify immunogenic regions within the **GbpB** sequence for use in subunit vaccines. Potential regions of immunogenicity were sought by use of a matrix-based algorithm (EpiMatrix) to estimate the binding characteristics of peptides derived from the **GbpB** sequence by using a database of known major histocompatibility complex class II binding alleles. Screening the entire sequence revealed several peptides with estimated high binding probabilities. Two N-terminal 20-mer peptides (SYI and QGQ) subtending two of these regions were synthesized. A preliminary experiment, in which these peptides were synthesized in the multiple antigenic peptide format and were used to subcutaneously immunize Sprague-Dawley rats twice at a 21-day interval, revealed that the SYI peptide induced a higher percentage of responses to the inciting peptide as well as to intact **GbpB**, as measured by enzyme-linked immunosorbent assay. The effect of immunization with the SYI peptide construct on the cariogenicity of S. mutans was then investigated by immunizing weanling Sprague-Dawley rats twice at a 9-day interval with SYI or with phosphate-buffered saline. All rats were then orally infected with S. mutans strain SJ. After a 78-day infection period, the SYI-immunized groups had significant reductions in dental caries on both smooth and occlusal surfaces compared with the sham-immunized group. Thus, these experiments indicated that at least one linear sequence, derived from the N-terminal third of **GbpB**, was sufficiently immunogenic to induce a protective immune response in this experimental rat model for dental caries.

L3 ANSWER 4 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2001:543227 BIOSIS
DN PREV200100543227
TI Cloning of the Streptococcus mutans gene encoding **glucan binding protein B** and analysis of genetic diversity and protein production in clinical isolates.
AU Mattos-Graner, Renata O.; Jin, Song; King, William F.; Chen, Tsute; **Smith, Daniel J.**; Duncan, Margaret J. [Reprint author]
CS Department of Molecular Genetics, Forsyth Institute, 140 Fenway, Boston, MA, 02115, USA
mduncan@forsyth.org
SO Infection and Immunity, (November, 2001) Vol. 69, No. 11, pp. 6931-6941. print.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 21 Nov 2001
Last Updated on STN: 25 Feb 2002
AB Streptococcus mutans, the primary etiological agent of dental caries, produces several activities that promote its accumulation within the dental biofilm. These include **glucosyltransferases**, their **glucan** products, and proteins that bind **glucan**. At least three **glucan** binding proteins have been identified, and **GbpB**, the protein characterized in this study, appears to be novel. The **gbpB** gene was cloned and the predicted protein sequence contained several unusual features and shared extensive homology with a putative peptidoglycan hydrolase from group B streptococcus. Examination of **gbpB** genes from clinical isolates of S. mutans revealed that DNA polymorphisms, and hence amino acid changes, were limited to the central region of the gene, suggesting functional conservation within the amino and carboxy termini of the protein. The **GbpB** produced by clinical isolates and laboratory strains showed various distributions between cells and culture medium, and amounts of protein produced by individual strains correlated positively with their ability to grow as biofilms in an in vitro assay.

L3 ANSWER 5 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2001:303013 BIOSIS
DN PREV200100303013

TI Passive transfer of immunoglobulin Y antibody to Streptococcus mutans **glucan binding protein B** can confer protection against experimental dental caries.
AU **Smith, Daniel J.** [Reprint author]; King, William F.; Godiska, Ronald
CS Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA, 02115, USA
dsmith@forsyth.org
SO Infection and Immunity, (May, 2001) Vol. 69, No. 5, pp. 3135-3142. print.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002
AB Active immunization with Streptococcus mutans **glucan binding protein B** (GBP-B) has been shown to induce protection against experimental dental caries. This protection presumably results from continuous secretion of salivary antibody to GBP-B, which inhibits accumulation of S. mutans within the oral biofilm. The purpose of this study was to explore the influence of short-term (9- or 24-day) passive oral administration of antibody to S. mutans GBP-B on the longer-term accumulation and cariogenicity of S. mutans in a rat model of dental caries. Preimmune chicken egg yolk immunoglobulin Y (IgY) or IgY antibody to S. mutans GBP-B was supplied in lower (experiment 1) and higher (experiment 2) concentrations in the diet and drinking water of rats for 9 (experiment 1) or 24 (experiment 2) days. During the first 3 days of IgY feeding, all animals were challenged with 5X106 streptomycin-resistant S. mutans strain SJ-r organisms. Rats remained infected with S. mutans for 78 days, during which rat molars were sampled for the accumulation of S. mutans SJ-r bacteria and total streptococci. Geometric mean levels of S. mutans SJ-r accumulation on molar surfaces were significantly lower in antibody-treated rats on days 16 and 78 of experiment 2 and were lower on all but the initial (day 5) swabbing occasions in both experiments. Relative to controls, the extent of molar dental caries measured on day 78 was also significantly decreased. The decrease in molar caries correlated with the amount and duration of antibody administration. This is the first demonstration that passive antibody to S. mutans GBP-B can have a protective effect against cariogenic S. mutans infection and disease. Furthermore, this decrease in infection and disease did not require continuous antibody administration for the duration of the infection period. This study also indicates that antibody to components putatively involved only in cellular aggregation can have a significant effect on the incorporation of mutans streptococci in dental biofilm.

L3 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:122595 CAPLUS
DN 142:217367
TI Immunogenic compositions for eliciting antibody production in mammals composed of fragments of Streptococcus **glucan binding protein-B** and **glucosyltransferase** isoenzymes
IN **Smith, Daniel J.**; Taubman, Martin A.
PA USA
SO U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 383,930.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005031633	A1	20050210	US 2004-797821	20040309
	US 6827936	B1	20041207	US 1999-290049	19990412
	US 2004127400	A1	20040701	US 2003-383930	20030307
PRAI	US 1998-81550P	P	19980413		
	US 1999-115142P	P	19990108		
	US 1999-290049	A2	19990412		
	US 2002-363209P	P	20020307		
	US 2002-402483P	P	20020808		
	US 2003-383930	A2	20030307		

AB The invention provides complete and partial sequences of various **GbpB** (**glucan binding protein-B**) proteins and **glucosyltransferase** (GTF) isoenzymes found in Streptococcus species, and the use of these sequences in construction of immunogenic compns. and vaccines. Specifically, the invention provides two different immunogenic compns. for eliciting production of antibodies in mammals composed of: (a) fragments of Streptococcus **GbpB** and a biocompatible microparticle; or (b) fragments of Streptococcus **GbpB** and GTF isoenzymes and a biocompatible microparticle. The invention relates that the **GbpB**-GTF composition further comprises a peptidyl core matrix containing lysines. The invention also relates that the disclosed **GbpB**-GTF chimeric protein may also contain a plurality of copies of the **GbpB** and GTF peptides. The invention also provides two specific **GbpB**-GTF diepitopic chimeric proteins: (a) SYI-GLU, which comprises S. mutans strain SJ32 **GbpB**-derived MHC class II SYI peptide and the **glucan** binding domain of GTF; and (b) SYI-CAT, which comprises S. mutans strain SJ32 **GbpB**-derived MHC class II SYI peptide and the catalytic domain of GTF. The invention further provides for the intranasal administration of said compns. into mammals for the induction of antibodies specific for GTF and **GbpB**. In the examples, the invention demonstrated that the SYI-GLU and SYI-CAT diepitopic constructs had enhanced antibody production in immunized rats. The invention also demonstrated dental caries protection by intranasal immunization with S. mutans **GbpB** peptide SYI.

L3 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:737524 CAPLUS
DN 139:259950
TI Streptococcal **glucan binding protein-B** and **glucosyltransferase** and fragments for inducing antibodies against dental caries
IN **Smith, Daniel J.**; Taubman, Martin A.
PA The Forsyth Institute, USA
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003075845	A2	20030918	WO 2003-US6962	20030307
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2480962	AA	20030918	CA 2003-2480962	20030307
	EP 1572149	A2	20050914	EP 2003-713953	20030307
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005531511	T2	20051020	JP 2003-574121	20030307
PRAI	US 2002-363209P	P	20020307		
	US 2002-402483P	P	20020808		
	WO 2003-US6962	W	20030307		

AB Immunogenic compns. and subunit vaccines for dental caries are described which comprise peptide subunits of **glucan binding protein-B** and peptide subunits of **glucan binding protein-B** in combination with peptide subunits of **glucosyltransferase**. Methods of provoking an immune response to S. mutans **glucan binding protein-B** or **glucosyltransferase**. Methods of immunizing a mammal against dental caries are also described, along with antibodies which bind particular epitopes of **glucan binding**

protein-B or **glucosyltransferase**.

L3 ANSWER 8 OF 8 USPATFULL on STN
AN 2004:165910 USPATFULL
TI Immunogenicity of **glucan** binding protein
IN **Smith, Daniel J.**, Natick, MA, UNITED STATES
Taubman, Martin A., Newtonville, MA, UNITED STATES
PI US 2004127400 A1 20040701
AI US 2003-383930 A1 20030307 (10)
PRAI US 2002-402483P 20020808 (60)
US 2002-363209P 20020307 (60)
DT Utility
FS APPLICATION
LREP Ingrid A. Beattie, Ph.D., Mintz, Levin, Cohn, Ferris, Glovsky and Popeo,P.C., One Financial Center, Boston, MA, 02111
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 3002
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Immunogenic compositions and subunit vaccines for dental caries are described which comprise peptide subunits of **glucan binding protein-B** and peptide subunits of **glucan binding protein-B** in combination with peptide subunits of **glucosyltransferase**. Methods of provoking an immune response to S. mutans **glucan binding protein-B** or **glucosyltransferase**. Methods of immunizing a mammal against dental caries are also described, along with antibodies which bind particular epitopes of **glucan binding protein-B** or **glucosyltransferase**.

```
=> e taubman martin A/au
E1          195     TAUBMAN MARK B/AU
E2            4     TAUBMAN MARTIN/AU
E3          121 --> TAUBMAN MARTIN A/AU
E4            1     TAUBMAN MATTHEW/AU
E5           19     TAUBMAN MATTHEW S/AU
E6            6     TAUBMAN MICHELE/AU
E7            1     TAUBMAN MITCHELL/AU
E8            1     TAUBMAN N A/AU
E9            1     TAUBMAN NORA E/AU
E10           2     TAUBMAN O/AU
E11          14     TAUBMAN P/AU
E12           1     TAUBMAN P D/AU

=> s e2-e3 and (glucan or glucosyltransferase?)
L4           63 ("TAUBMAN MARTIN"/AU OR "TAUBMAN MARTIN A"/AU) AND (GLUCAN OR
                GLUCOSYLTRANSFERASE?)

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5           40 DUP REM L4 (23 DUPLICATES REMOVED)

=> s l5 and ((GbpB)or(glucan binding protein B))
L6            5 L5 AND ((GBPB) OR(GLUCAN BINDING PROTEIN B))

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y
```

L6 ANSWER 1 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2005:278296 BIOSIS
DN PREV200510068959
TI Immunological and protective effects of diepitopic subunit dental caries vaccines.
AU Smith, Daniel J. [Reprint Author]; King, William F.; Rivero, Joy; **Taubman, Martin A.**

CS Forsyth Inst, Dept Immunol, 140 Fenway, Boston, MA 02115 USA
dsmith@forsyth.org
SO Infection and Immunity, (MAY 2005) Vol. 73, No. 5, pp. 2797-2804.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 27 Jul 2005
Last Updated on STN: 27 Jul 2005
AB As a prelude to development of broader-spectrum vaccines for dental caries, we explored the immune potential of constructs combining epitopes from mutans streptococcal **glucosyltransferases** (GTF) and **glucan binding protein B** (**GbpB**). Two diepitopic peptide constructs were synthesized in a multiple antigenic peptide (MAP) format. Both constructs contained SYI, a 20-mer **GbpB** peptide that included a sequence having major histocompatibility complex class 11 binding characteristics. One diepitopic construct (SYI-CAT) also contained a 22-mer sequence from the catalytic domain of GTF. Another diepitopic construct (SYI-GLU) contained a 22-mer sequence from the **glucan** binding domain of GTF. To assess the ability of each construct to induce antibody reactive with **GbpB** and GTF native proteins, rats were injected subcutaneously with SYI-CAT, SYI-GLU, or the constituent monoepitopic constructs. Only the SYI-CAT construct induced significant levels of serum immunoglobulin G (IgG) and IgA antibody to both pathogenesis-associated proteins. Also, immunization with SYI-CAT significantly ($P < 0.001$) enhanced the antibody response to the CAT peptide. Experiments then compared experimental dental caries after immunization with SYI-CAT, SYI, or CAT MAP constructs, followed by infection with Streptococcus mutans strain SJr. Dental caries were lower in each peptide-immunized group than in the sham-injected group. The level of protection after SYI-CAT immunization was similar to that after immunization with constituent MAP constructs. In another experiment, rats were infected with Streptococcus sobrinus strain 6715 under an identical protocol. Significant protection was observed on buccal surfaces in both SYI-CAT and CAT construct-immunized, but not in the SYI construct-immunized, groups. Thus, addition of the **GbpB** -derived SYI peptide to the GTF-derived CAT peptide construct not only enhanced the immunological response to CAT and GTF epitopes, but also extended the protective effect of the construct to include both S. mutans and S. sobrinus.

L6 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2003:172182 BIOSIS
DN PREV200300172182
TI Immunogenicity and protective immunity induced by synthetic peptides associated with putative immunodominant regions of Streptococcus mutans **glucan-binding protein B.**
AU Smith, Daniel J. [Reprint Author]; King, William F.; Barnes, Leigh A.; Peacock, Zachary; **Taubman, Martin A.**
CS Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA, 02115, USA
dsmith@forsyth.org
SO Infection and Immunity, (March 2003) Vol. 71, No. 3, pp. 1179-1184. print.
ISSN: 0019-9567 (ISSN print).
DT Article
LA English
ED Entered STN: 2 Apr 2003
Last Updated on STN: 2 Apr 2003
AB **Glucan-binding protein B** (**GbpB**) from Streptococcus mutans has been shown to induce protective immunity to dental caries in experimental models. Having recently sequenced the **gbpB** gene, our objective in this study was to identify immunogenic regions within the **GbpB** sequence for use in subunit vaccines. Potential regions of immunogenicity were sought by use of a matrix-based algorithm (EpiMatrix) to estimate the binding characteristics of peptides derived from the **GbpB** sequence by using a database of known major histocompatibility complex class II binding alleles. Screening the entire sequence revealed several peptides with estimated high binding probabilities. Two N-terminal 20-mer peptides (SYI and QGQ) subtending two of these regions were synthesized. A

preliminary experiment, in which these peptides were synthesized in the multiple antigenic peptide format and were used to subcutaneously immunize Sprague-Dawley rats twice at a 21-day interval, revealed that the SYI peptide induced a higher percentage of responses to the inciting peptide as well as to intact **GbpB**, as measured by enzyme-linked immunosorbent assay. The effect of immunization with the SYI peptide construct on the cariogenicity of S. mutans was then investigated by immunizing weanling Sprague-Dawley rats twice at a 9-day interval with SYI or with phosphate-buffered saline. All rats were then orally infected with S. mutans strain SJ. After a 78-day infection period, the SYI-immunized groups had significant reductions in dental caries on both smooth and occlusal surfaces compared with the sham-immunized group. Thus, these experiments indicated that at least one linear sequence, derived from the N-terminal third of **GbpB**, was sufficiently immunogenic to induce a protective immune response in this experimental rat model for dental caries.

L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:122595 CAPLUS
DN 142:217367
TI Immunogenic compositions for eliciting antibody production in mammals composed of fragments of Streptococcus **glucan binding protein-B** and **glucosyltransferase** isoenzymes
IN Smith, Daniel J.; **Taubman, Martin A.**
PA USA
SO U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 383,930.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005031633	A1	20050210	US 2004-797821	20040309
	US 6827936	B1	20041207	US 1999-290049	19990412
	US 2004127400	A1	20040701	US 2003-383930	20030307
PRAI	US 1998-81550P	P	19980413		
	US 1999-115142P	P	19990108		
	US 1999-290049	A2	19990412		
	US 2002-363209P	P	20020307		
	US 2002-402483P	P	20020808		
	US 2003-383930	A2	20030307		

AB The invention provides complete and partial sequences of various **GbpB** (**glucan binding protein-B**) proteins and **glucosyltransferase** (GTF) isoenzymes found in Streptococcus species, and the use of these sequences in construction of immunogenic compns. and vaccines. Specifically, the invention provides two different immunogenic compns. for eliciting production of antibodies in mammals composed of: (a) fragments of Streptococcus **GbpB** and a biocompatible microparticle; or (b) fragments of Streptococcus **GbpB** and GTF isoenzymes and a biocompatible microparticle. The invention relates that the **GbpB**-GTF composition further comprises a peptidyl core matrix containing lysines. The invention also relates that the disclosed **GbpB**-GTF chimeric protein may also contain a plurality of copies of the **GbpB** and GTF peptides. The invention also provides two specific **GbpB**-GTF diepitopic chimeric proteins: (a) SYI-GLU, which comprises S. mutans strain SJ32 **GbpB**-derived MHC class II SYI peptide and the **glucan** binding domain of GTF; and (b) SYI-CAT, which comprises S. mutans strain SJ32 **GbpB**-derived MHC class II SYI peptide and the catalytic domain of GTF. The invention further provides for the intranasal administration of said compns. into mammals for the induction of antibodies specific for GTF and **GbpB**. In the examples, the invention demonstrated that the SYI-GLU and SYI-CAT diepitopic constructs had enhanced antibody production in immunized rats. The invention also demonstrated dental caries protection by intranasal immunization with S. mutans **GbpB** peptide SYI.

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:737524 CAPLUS

DN 139:259950
TI Streptococcal **glucan binding protein-B** and **glucosyltransferase** and fragments for inducing antibodies against dental caries
IN Smith, Daniel J.; **Taubman, Martin A.**
PA The Forsyth Institute, USA
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003075845	A2	20030918	WO 2003-US6962	20030307
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2480962	AA	20030918	CA 2003-2480962	20030307
	EP 1572149	A2	20050914	EP 2003-713953	20030307
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005531511	T2	20051020	JP 2003-574121	20030307
PRAI	US 2002-363209P	P	20020307		
	US 2002-402483P	P	20020808		
	WO 2003-US6962	W	20030307		

AB Immunogenic compns. and subunit vaccines for dental caries are described which comprise peptide subunits of **glucan binding protein-B** and peptide subunits of **glucan binding protein-B** in combination with peptide subunits of **glucosyltransferase**. Methods of provoking an immune response to S. mutans **glucan binding protein -B** or **glucosyltransferase**. Methods of immunizing a mammal against dental caries are also described, along with antibodies which bind particular epitopes of **glucan binding protein-B** or **glucosyltransferase**.

L6 ANSWER 5 OF 5 USPATFULL on STN
AN 2004:165910 USPATFULL
TI Immunogenicity of **glucan** binding protein
IN Smith, Daniel J., Natick, MA, UNITED STATES
Taubman, Martin A., Newtonville, MA, UNITED STATES
PI US 2004127400 A1 20040701
AI US 2003-383930 A1 20030307 (10)
PRAI US 2002-402483P 20020808 (60)
US 2002-363209P 20020307 (60)
DT Utility
FS APPLICATION
LREP Ingrid A. Beattie, Ph.D., Mintz, Levin, Cohn, Ferris, Glovsky and Popeo,P.C., One Financial Center, Boston, MA, 02111
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 3002
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Immunogenic compositions and subunit vaccines for dental caries are described which comprise peptide subunits of **glucan binding protein-B** and peptide subunits of **glucan binding protein-B** in combination with peptide subunits of **glucosyltransferase**. Methods of provoking an immune response to S. mutans **glucan binding protein-B** or **glucosyltransferase**. Methods of immunizing a mammal against

dental caries are also described, along with antibodies which bind particular epitopes of **glucan binding protein-B** or **glucosyltransferase**.

```
=> s (glucan or glucosyltransferase?)and((glucan binding protein B)or(GbpB))
L7          56 (GLUCAN OR GLUCOSYLTRANSFERASE?) AND((GLUCAN BINDING PROTEIN B)
               OR(GBPB))

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8          18 DUP REM L7 (38 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 18 ANSWERS - CONTINUE? Y/(N):y

L8   ANSWER 1 OF 18     MEDLINE on STN                  DUPLICATE 1
AN   2006005869     IN-PROCESS
DN   PubMed ID: 16390340
TI   Binding of glucan-binding protein C to GTFD-synthesized soluble
     glucan in sucrose-dependent adhesion of Streptococcus mutans.
AU   Matsumoto M; Fujita K; Ooshima T
CS   Department of Pediatric Dentistry, Osaka University Graduate School of
     Dentistry, Osaka, Japan.
SO   Oral microbiology and immunology, (2006 Feb) 21 (1) 42-6.
     Journal code: 8707451. ISSN: 0902-0055.
CY   Denmark
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Dental Journals
ED   Entered STN: 20060105
     Last Updated on STN: 20060105
AB   Streptococcus mutans produces glucan-binding proteins (Gbp
     proteins) which promote the adhesion of the organism to teeth.  Three Gbp
     proteins, GbpA protein, GbpB protein, and GbpC protein have been
     identified; however, the mechanism of adhesion between glucans and
     bacterial cell surfaces is unknown.  We used glucosyltransferase
     (GTF)- and/or Gbp-deficient mutants to examine the role of GbpC protein in
     the sucrose-dependent cellular adhesion of S. mutans to glass surfaces.
     The wild-type strain MT8148 and a GbpA-deficient mutant strain displayed
     increased sucrose-dependent adhesion following the addition of rGTFD.
     However, a GbpC-deficient mutant strain demonstrated no changes in the
     level of sucrose-dependent adhesion in spite of the addition of rGTFD.
     Further, the binding of rGbpC protein to the glucan synthesized
     by rGTFD was significantly higher than that to the glucan
     synthesized by either rGTFB or rGTFC.  These results suggest that GbpC
     protein may play an important role in sucrose-dependent adhesion by
     binding to the soluble glucan synthesized by GTFD.

L8   ANSWER 2 OF 18  CAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 2
AN   2005:122595  CAPLUS
DN   142:217367
TI   Immunogenic compositions for eliciting antibody production in mammals
     composed of fragments of Streptococcus glucan binding
     protein-B and glucosyltransferase isoenzymes
IN   Smith, Daniel J.; Taubman, Martin A.
PA   USA
SO   U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 383,930.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 4
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     --------------      ----   --------    --------------------     --------
PI   US 2005031633        A1    20050210    US 2004-797821           20040309
     US 6827936           B1    20041207    US 1999-290049           19990412
     US 2004127400        A1    20040701    US 2003-383930           20030307
PRAI US 1998-81550P       P     19980413
     US 1999-115142P      P     19990108
```

US 1999-290049 A2 19990412
US 2002-363209P P 20020307
US 2002-402483P P 20020808
US 2003-383930 A2 20030307

AB The invention provides complete and partial sequences of various **GbpB** (**glucan binding protein-B**) proteins and **glucosyltransferase** (GTF) isoenzymes found in Streptococcus species, and the use of these sequences in construction of immunogenic compns. and vaccines. Specifically, the invention provides two different immunogenic compns. for eliciting production of antibodies in mammals composed of: (a) fragments of Streptococcus **GbpB** and a biocompatible microparticle; or (b) fragments of Streptococcus **GbpB** and GTF isoenzymes and a biocompatible microparticle. The invention relates that the **GbpB**-GTF composition further comprises a peptidyl core matrix containing lysines. The invention also relates that the disclosed **GbpB**-GTF chimeric protein may also contain a plurality of copies of the **GbpB** and GTF peptides. The invention also provides two specific **GbpB**-GTF diepitopic chimeric proteins: (a) SYI-GLU, which comprises S. mutans strain SJ32 **GbpB**-derived MHC class II SYI peptide and the **glucan** binding domain of GTF; and (b) SYI-CAT, which comprises S. mutans strain SJ32 **GbpB**-derived MHC class II SYI peptide and the catalytic domain of GTF. The invention further provides for the intranasal administration of said compns. into mammals for the induction of antibodies specific for GTF and **GbpB**. In the examples, the invention demonstrated that the SYI-GLU and SYI-CAT diepitopic constructs had enhanced antibody production in immunized rats. The invention also demonstrated dental caries protection by intranasal immunization with S. mutans **GbpB** peptide SYI.

L8 ANSWER 3 OF 18 USPATFULL on STN
AN 2005:331878 USPATFULL
TI Computational method for identifying adhesin and adhesin-like proteins of therapeutic potential
IN Sachdeva, Gaurav, Delhi, INDIA
Kumar, Kaushal, Delhi, INDIA
Jain, Preti, Delhi, INDIA
Brahmachari, Samir K., Delhi, INDIA
Ramachandran, Srinivasan, Delhi, INDIA
PA COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH, New Delhi, INDIA (non-U.S. corporation)
PI US 2005288866 A1 20051229
AI US 2005-52554 A1 20050207 (11)
PRAI IN 2004-1732004 20040206
US 2004-589227P 20040720 (60)
DT Utility
FS APPLICATION
LREP MARSHALL, GERSTEIN & BORUN LLP, 233 S. WACKER DRIVE, SUITE 6300, SEARS TOWER, CHICAGO, IL, 60606, US
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 1730
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A computational method for identifying adhesin and adhesin-like proteins, said method comprising steps of computing the sequence-based attributes of a neural network software wherein the attributes are (i) amino acid frequencies, (ii) multiplet frequency, (iii) dipeptide frequencies, (iv),charge composition, and (v) hydrophobic composition, training the artificial neural Network (ANN) for each of the computed five attributes, and identifying the adhesin and adhesin-like proteins having probability of being an adhesin (P.sub.ad) as ≥0.51; a computer system for performing the method; and genes and proteins encoding adhesin and adhesin-like proteins.

L8 ANSWER 4 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 3
AN 2005:554664 BIOSIS
DN PREV200510340130

TI Role of HtrA in surface protein expression and biofilm formation by Streptococcus mutans.
AU Biswas, Saswati; Biswas, Indranil [Reprint Author]
CS Univ S Dakota, Sch Med, Div Basic Biomed Sci, Lee Med Bldg,414 E Clark St, Vermillion, SD 57069 USA
ibiswas@usd.edu
SO Infection and Immunity, (OCT 2005) Vol. 73, No. 10, pp. 6923-6934.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
OS GenBank-AE004092; EMBL-AE004092; DDJB-AE004092; GenBank-AE015037; EMBL-AE015037; DDJB-AE015037; GenBank-NC004350; EMBL-NC004350; DDJB-NC004350; GenBank-NC003098; EMBL-NC003098; DDJB-NC003098; GenBank-NC002662; EMBL-NC002662; DDJB-NC002662
ED Entered STN: 7 Dec 2005
Last Updated on STN: 7 Dec 2005
AB The HtrA surface protease in gram-positive bacteria is involved in the processing and maturation of extracellular proteins and degradation of abnormal or misfolded proteins. Inactivation of htrA has been shown to affect the tolerance to thermal and environmental stress and to reduce virulence. We found that inactivation of Streptococcus mutans htrA by gene-replacement also resulted in a reduced ability to withstand exposure to low and high temperatures, low pH, and oxidative and DNA damaging agents. The htrA mutation affected surface expression of several extracellular proteins including **glucan-binding protein B (GbpB)**, **glucosyltransferases**, and fructosyltransferase. In addition, htrA mutation also altered the surface expression of enolase and glyceraldehyde-3-phosphate dehydrogenease, two glycolytic enzymes that are known to be present on the streptococcal cell surface. As expected, microscopic analysis of in vitro grown biofilm structure revealed that the htrA deficient biofilms adopted a much more granular patchy appearance, rather than the relatively smooth confluent layer normally seen in the wild type. These results suggest that HtrA plays an important role in the biogenesis of extracellular proteins including surface associated glycolytic enzymes and in biofilm formation of S. mutans.

L8 ANSWER 5 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 4
AN 2005:498381 BIOSIS
DN PREV200510279091
TI Characterization of salivary immunoglobulin A responses in children heavily exposed to the oral bacterium Streptococcus mutans: Influence of specific antigen recognition in infection.
AU Nogueira, Ruchele D.; Alves, Alessandra C.; Napimoga, Marcelo H.; Smith, Daniel J.; Mattos-Graner, Renata O. [Reprint Author]
CS UNICAMP, Fac Odontol Piracicaba, Dept Microbiol and Imunol, Piracicaba Sch Dent, Av Limeira 901, BR-13414903 Sao Paulo, Brazil
rmgraner@fop.unicamp.br
SO Infection and Immunity, (SEP 2005) Vol. 73, No. 9, pp. 5675-5684.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005
AB The initial infection of children by Streptococcus mutans, the main pathogen of dental caries, depends on the ability of S. mutans to adhere and accumulate on tooth surfaces. These processes involve the adhesin antigen I/II (AgI/II), **glucosyltransferases** (GTF) and **glucan-binding protein B** (**GbpB**), each a target for anticaries vaccines. The salivary immunoglobulin A (IgA) antibody responses to S. mulans antigens (Ags) were characterized in 21 pairs of 5- to 13-month-old children. Pairs were constructed with one early S. mutans-infected and one noninfected child matched by age, racial background, number of teeth, and salivary levels of IgA. Specific salivary IgA antibody response and S. mutans infection levels were then measured during a I-year follow-up. Robust responses to S. mutans were detected from 6 months of age. Salivary IgA antibody to AgI/II and GTF was commonly detected in salivas of all 42 children.

However, **GbpB**-specific IgA antibody was seldom detected in the subset of infected children (38.1% at baseline). In contrast, most of the subset of noninfected children (76.2%) showed **GbpB**-reactive IgA antibody during the same period. Frequencies of **GbpB** responses increased with age, but differences in intensities of **GbpB**-IgA antibody reactions were sustained between the subsets. At baseline, **GbpB**-reactive IgA antibody accounted for at least half of the total salivary IgA S. mutans-reactive antibody in 33.3 and 9.5% of noninfected and infected children, respectively. This study provides evidence that a robust natural response to S. mutans Ags can be achieved by 1 year of age and that IgA antibody specificities may be critical in modulating initial S. mutans infection.

L8 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
AN 2005:531713 CAPLUS
DN 143:208717
TI A VicRK signal transduction system in Streptococcus mutans affects gtfBCD, **gbpB**, and ftf expression, biofilm formation, and genetic competence development
AU Senadheera, M. Dilani; Guggenheim, Bernard; Spatafora, Grace A.; Huang, Yi-Chen Cathy; Choi, Jison; Hung, David C. I.; Treglown, Jennifer S.; Goodman, Steven D.; Ellen, Richard P.; Cvitkovitch, Dennis G.
CS Dental Research Institute, University of Toronto, Toronto, ON, M51G6, Can.
SO Journal of Bacteriology (2005), 187(12), 4064-4076
CODEN: JOBAAY; ISSN: 0021-9193
PB American Society for Microbiology
DT Journal
LA English
AB Bacteria exposed to transient host environments can elicit adaptive responses by triggering the differential expression of genes via two-component signal transduction systems. This study describes the vicRK signal transduction system in Streptococcus mutans. A vicK (putative histidine kinase) deletion mutant (SmuvicK) was isolated. However, a vicR (putative response regulator) null mutation was apparently lethal, since the only transformants isolated after attempted mutagenesis overexpressed all three genes in the vicRKX operon (Smuvic+). Compared with the wild-type UA159 strain, both mutants formed aberrant biofilms. Moreover, the vicK mutant biofilm formed in sucrose-supplemented medium was easily detachable relative to that of the parent. The rate of total dextran formation by this mutant was remarkably reduced compared to the wild type, whereas it was increased in Smuvic+. Based on real-time PCR, Smuvic+ showed increased gtfBCD, **gbpB**, and ftf expression, while a recombinant VicR fusion protein was shown to bind the promoter regions of the gtfB, gtfC, and ftf genes. Also, transformation efficiency in the presence or absence of the S. mutans competence-stimulating peptide was altered for the vic mutants. In vivo studies conducted using SmuvicK in a specific-pathogen-free rat model resulted in significantly increased smooth-surface dental plaque (Pearson-Filon statistic [PF], < 0.001). While the absence of vicK did not alter the incidence of caries, a significant reduction in SmuvicK CFU counts was observed in plaque samples relative to that of the parent (PF, < 0.001). Taken together, these findings support involvement of the vicRK signal transduction system in regulating several important physiol. processes in S. mutans.
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 6
AN 2005:278296 BIOSIS
DN PREV200510068959
TI Immunological and protective effects of diepitopic subunit dental caries vaccines.
AU Smith, Daniel J. [Reprint Author]; King, William F.; Rivero, Joy; Taubman, Martin A.
CS Forsyth Inst, Dept Immunol, 140 Fenway, Boston, MA 02115 USA
dsmith@forsyth.org
SO Infection and Immunity, (MAY 2005) Vol. 73, No. 5, pp. 2797-2804.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article

LA English
ED Entered STN: 27 Jul 2005
Last Updated on STN: 27 Jul 2005
AB As a prelude to development of broader-spectrum vaccines for dental caries, we explored the immune potential of constructs combining epitopes from mutans streptococcal **glucosyltransferases** (GTF) and **glucan binding protein B** (**GbpB**). Two diepitopic peptide constructs were synthesized in a multiple antigenic peptide (MAP) format. Both constructs contained SYI, a 20-mer **GbpB** peptide that included a sequence having major histocompatibility complex class 11 binding characteristics. One diepitopic construct (SYI-CAT) also contained a 22-mer sequence from the catalytic domain of GTF. Another diepitopic construct (SYI-GLU) contained a 22-mer sequence from the **glucan** binding domain of GTF. To assess the ability of each construct to induce antibody reactive with **GbpB** and GTF native proteins, rats were injected subcutaneously with SYI-CAT, SYI-GLU, or the constituent monoepitopic constructs. Only the SYI-CAT construct induced significant levels of serum immunoglobulin G (IgG) and IgA antibody to both pathogenesis-associated proteins. Also, immunization with SYI-CAT significantly ($P < 0.001$) enhanced the antibody response to the CAT peptide. Experiments then compared experimental dental caries after immunization with SYI-CAT, SYI, or CAT MAP constructs, followed by infection with Streptococcus mutans strain SJr. Dental caries were lower in each peptide-immunized group than in the sham-injected group. The level of protection after SYI-CAT immunization was similar to that after immunization with constituent MAP constructs. In another experiment, rats were infected with Streptococcus sobrinus strain 6715 under an identical protocol. Significant protection was observed on buccal surfaces in both SYI-CAT and CAT construct-immunized, but not in the SYI construct-immunized, groups. Thus, addition of the **GbpB** -derived SYI peptide to the GTF-derived CAT peptide construct not only enhanced the immunological response to CAT and GTF epitopes, but also extended the protective effect of the construct to include both S. mutans and S. sobrinus.

L8 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1342490 CAPLUS
TI Preliminary study of pcDNA3.1 (+)-**gbpB**-chitosan nanoparticles as a novel nasal delivery system for anti-carious vaccine
AU Wei, Kewen; Fan, Mingwen; Wu, Buling
CS School of Stomatology, Wuhan University, Wuhan, 430079, Peop. Rep. China
SO Wuhan Daxue Xuebao, Yixueban (2005), 26(3), 351-354
CODEN: WDXYAA; ISSN: 1671-8852
PB Wuhan Daxue Qikanshe
DT Journal
LA Chinese
AB The effect of intranasal administration of pcDNA3.1 (+)-**gbpB** -chitosan nanoparticles on the systemic and mucosal immune response was examined Two formulations of pcDNA3.1 (+)-**gbpB**-chitosan nanoparticles were prepared and administrated to immunize Sprague-Dawley (SD) rats through the nasal. Serum and salivary samples were collected periodically, **GbpB**-specific IgG and IgA antibodies were measured by an adapted method ELISA (ELISA). The system and local immune response were significantly higher than that observed as the neg. controls. The chitosan nanoparticles formulated in this study were suitable for the intranasal anti-carious plasmid DNA vaccine delivery.

L8 ANSWER 9 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 7
AN 2005:132142 BIOSIS
DN PREV200500133041
TI Influence of microparticle formulation on immunogenicity of SYI, a synthetic peptide derived from Streptococcus mutans **GbpB**.
AU Peacock, Z. S.; Barnes, L. A.; King, W. F.; Trantolo, D. J.; Wise, D. L.; Taubman, M. A.; Smith, D. J. [Reprint Author]
CS Dept Immunol, Forsyth Inst, 140 Fenway, Boston, MA, 02115, USA
SO Oral Microbiology and Immunology, (February 2005) Vol. 20, No. 1, pp. 60-64. print.
ISSN: 0902-0055 (ISSN print).

DT Article
LA English
ED Entered STN: 6 Apr 2005
Last Updated on STN: 6 Apr 2005
AB Subcutaneous immunization with SYI, a peptide construct based on Streptococcus mutans **glucan binding protein B** (**GbpB**) residues 113-132, significantly reduces experimental dental caries. Since mucosal immunization may be preferred for human vaccine applications, the present objective was to determine what formulation of SYI combined with polylactide-coglycolide microparticles could give rise to significant levels of salivary IgA antibody reactive with the native **GbpB** protein. A comparison of the SYI construct, loaded into or mixed with polylactide-coglycolide revealed the SYI-loaded microparticles to induce significant and sustainable levels of salivary and nasal wash IgA antibody to the peptide and the native protein. SYI mixed with unloaded microparticles was less effective in mucosal antibody response induction. These studies indicate that mucosal immunization with the SYI construct can induce salivary IgA antibody to a pathogenesis-associated component of S. mutans if delivered within polylactide-coglycolide microparticles, suggesting that this approach could successfully induce protective salivary immunity to dental caries caused by S. mutans.

L8 ANSWER 10 OF 18 USPATFULL on STN
AN 2004:165910 USPATFULL
TI Immunogenicity of **glucan** binding protein
IN Smith, Daniel J., Natick, MA, UNITED STATES
Taubman, Martin A., Newtonville, MA, UNITED STATES
PI US 2004127400 A1 20040701
AI US 2003-383930 A1 20030307 (10)
PRAI US 2002-402483P 20020808 (60)
US 2002-363209P 20020307 (60)
DT Utility
FS APPLICATION
LREP Ingrid A. Beattie, Ph.D., Mintz, Levin, Cohn, Ferris, Glovsky and Popeo,P.C., One Financial Center, Boston, MA, 02111
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 3002
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Immunogenic compositions and subunit vaccines for dental caries are described which comprise peptide subunits of **glucan binding protein-B** and peptide subunits of **glucan binding protein-B** in combination with peptide subunits of **glucosyltransferase**. Methods of provoking an immune response to S. mutans **glucan binding protein-B** or **glucosyltransferase**. Methods of immunizing a mammal against dental caries are also described, along with antibodies which bind particular epitopes of **glucan binding protein-B** or **glucosyltransferase**.

L8 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8
AN 2005:197678 CAPLUS
DN 142:480327
TI Establishment of gene vaccine for caries prevention in the cells of mammals and its expression characteristics
AU Wei, Kewen; Wu, Buling; Xiao, Mingzhen; Su, Lingyun
CS College of Stomatology, Fourth Military Medical University, Xian, Shaanxi Province, 710032, Peop. Rep. China
SO Zhongguo Linchuang Kangfu (2004), 8(14), 2750-2751, 1 plate
CODEN: ZLKHAH; ISSN: 1671-5926
PB Zhongguo Linchuang Kangfu Zazhishe
DT Journal
LA English
AB The expression of **glucan-binding protein B** (**gbpB**) eukaryotic expression plasmid in the COS-7 cells of mammals was observed Eukaryotic expression plasmid pcDNA3.1(+)-

gbpB was established by gene recombinant technique, and was transfected into COS-7 cells by liposome method. The expression of plasmid pcDNA3.1(+)-**gbpB** in COS-7 cells was assayed by immunohistochem. SABC method and DAB staining. The cytoplasm of the COS-7 cells transfected by pcDNA3.1 (+)-**gbpB** plasmid showed a light brown staining, and there was no staining in the nucleus. There was no staining in the cytoplasm and nucleus of the cells transfected by pcDNA3.1(+) empty carrier as well as those in the control group. Plasmid pcDNA3.1(+)-**gbpB** can be translated and expressed in COS-7 cells after transfection. The expressed protein is in cytoplasm, and can bind with anti-**gbpB** specific antibody. Therefore, the plasmid pcDNA3.1(+)-**gbpB** with antigenicity can be used as a gene vaccine.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:737524 CAPLUS
DN 139:259950
TI Streptococcal **glucan binding protein-B** and **glucosyltransferase** and fragments for inducing antibodies against dental caries
IN Smith, Daniel J.; Taubman, Martin A.
PA The Forsyth Institute, USA
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003075845	A2	20030918	WO 2003-US6962	20030307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2480962	AA	20030918	CA 2003-2480962	20030307
EP 1572149	A2	20050914	EP 2003-713953	20030307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005531511	T2	20051020	JP 2003-574121	20030307
PRAI US 2002-363209P	P	20020307		
US 2002-402483P	P	20020808		
WO 2003-US6962	W	20030307		

AB Immunogenic compns. and subunit vaccines for dental caries are described which comprise peptide subunits of **glucan binding protein-B** and peptide subunits of **glucan binding protein-B** in combination with peptide subunits of **glucosyltransferase**. Methods of provoking an immune response to S. mutans **glucan binding protein -B** or **glucosyltransferase**. Methods of immunizing a mammal against dental caries are also described, along with antibodies which bind particular epitopes of **glucan binding protein-B** or **glucosyltransferase**.

L8 ANSWER 13 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 9
AN 2003:172182 BIOSIS
DN PREV200300172182
TI Immunogenicity and protective immunity induced by synthetic peptides associated with putative immunodominant regions of Streptococcus mutans **glucan-binding protein B**.
AU Smith, Daniel J. [Reprint Author]; King, William F.; Barnes, Leigh A.;

Peacock, Zachary; Taubman, Martin A.
CS Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA, 02115, USA
dsmith@forsyth.org
SO Infection and Immunity, (March 2003) Vol. 71, No. 3, pp. 1179-1184. print.
ISSN: 0019-9567 (ISSN print).
DT Article
LA English
ED Entered STN: 2 Apr 2003
Last Updated on STN: 2 Apr 2003
AB **Glucan-binding protein B** (
GbpB) from Streptococcus mutans has been shown to induce protective immunity to dental caries in experimental models. Having recently sequenced the **gbpB** gene, our objective in this study was to identify immunogenic regions within the **GbpB** sequence for use in subunit vaccines. Potential regions of immunogenicity were sought by use of a matrix-based algorithm (EpiMatrix) to estimate the binding characteristics of peptides derived from the **GbpB** sequence by using a database of known major histocompatibility complex class II binding alleles. Screening the entire sequence revealed several peptides with estimated high binding probabilities. Two N-terminal 20-mer peptides (SYI and QGQ) subtending two of these regions were synthesized. A preliminary experiment, in which these peptides were synthesized in the multiple antigenic peptide format and were used to subcutaneously immunize Sprague-Dawley rats twice at a 21-day interval, revealed that the SYI peptide induced a higher percentage of responses to the inciting peptide as well as to intact **GbpB**, as measured by enzyme-linked immunosorbent assay. The effect of immunization with the SYI peptide construct on the cariogenicity of S. mutans was then investigated by immunizing weanling Sprague-Dawley rats twice at a 9-day interval with SYI or with phosphate-buffered saline. All rats were then orally infected with S. mutans strain SJ. After a 78-day infection period, the SYI-immunized groups had significant reductions in dental caries on both smooth and occlusal surfaces compared with the sham-immunized group. Thus, these experiments indicated that at least one linear sequence, derived from the N-terminal third of **GbpB**, was sufficiently immunogenic to induce a protective immune response in this experimental rat model for dental caries.

L8 ANSWER 14 OF 18 EMBASE
AN 2003014640 EMBASE
TI Dental caries vaccines: Prospects and concerns.
AU Smith D.J.
CS D.J. Smith, Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA 02115, United States. dsmith@forsyth.org
SO Critical Reviews in Oral Biology and Medicine, (2002) Vol. 13, No. 4, pp. 335-349.
Refs: 155
ISSN: 1045-4411 CODEN: CROMEF
CY United States
DT Journal; General Review
FS 037 Drug Literature Index
039 Pharmacy
LA English
SL English
ED Entered STN: 20030116
Last Updated on STN: 20030116
AB Dental caries remains one of the most common infectious diseases of mankind. Cariogenic micro-organisms enter the dental biofilm early in life and can subsequently emerge, under favorable environmental conditions, to cause disease. In oral fluids, adaptive host defenses aroused by these infections are expressed in the saliva and gingival crevicular fluid. This review will focus on methods by which mucosal host defenses can be induced by immunization to interfere with dental caries caused by mutans streptococci. The natural history of mutans streptococcal colonization is described in the context of the ontogeny of mucosal immunity to these and other indigenous oral streptococci. Molecular targets for dental caries vaccines are explored for their

effectiveness in intact protein and subunit (synthetic peptide, recombinant and conjugate) vaccines in pre-clinical studies. Recent progress in the development of mucosal adjuvants and viable and non-viable delivery systems for dental caries vaccines is described. Finally, the results of clinical trials are reviewed, followed by a discussion of the prospects and concerns of human application of the principles presented.

L8 ANSWER 15 OF 18 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2002:592977 SCISEARCH
GA The Genuine Article (R) Number: 559KE
TI Mutant analysis of the gene encoding **glucan binding protein B** indicates an essential role in Streptococcus mutans
AU Mattos-Graner R O (Reprint); Zucchi P; Smith D J; Duncan M J
SO JOURNAL OF DENTAL RESEARCH, (MAR 2002) Vol. 81, Sp. iss. SI, pp. A40-A40. MA 0091.
ISSN: 0022-0345.
PB INT AMER ASSOC DENTAL RESEARCHI A D R/A A D R, 1619 DUKE ST, ALEXANDRIA, VA 22314-3406 USA.
DT Conference; Journal
LA English
REC Reference Count: 0
ED Entered STN: 2 Aug 2002
Last Updated on STN: 2 Aug 2002

L8 ANSWER 16 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 2003:272625 BIOSIS
DN PREV200300272625
TI 80th General Session of the IADR, 31st Annual Meeting of the AADR, and the 26th Annual Meeting of the CADR, San Diego, California, USA, March 6-9, 2002.
AU Anonymous
SO Journal of Dental Research, (March 2002) Vol. 81, No. Special Issue A, pp. A1-A568. print.
Meeting Info.: 80th General Session of the IADR, 31st AnnualMeeting of the AADR, and the 26th Annual Meeting of the CADR. San Diego, California, USA. March 06-09, 2002.
CODEN: JDREAF. ISSN: 0022-0345.
DT Conference; (Meeting)
Conference; (Meeting Summary)
LA English
ED Entered STN: 11 Jun 2003
Last Updated on STN: 11 Jun 2003
AB This meeting on dental research consists of abstracts written in English for 4,155 presentations and posters. Session themes cover biocompatibility of dental materials, periodontal medicine during pregnancy, enamel proteins, risk factors for tooth loss, and saliva in health and disease. Selected topics include gene encoding **glucan -binding protein B**, anticancer effect of lentiviral vector, masticatory muscle activity, HIV-related dysplasic warts, and fungicidal activity of zinc.

L8 ANSWER 17 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 10
AN 2001:543227 BIOSIS
DN PREV200100543227
TI Cloning of the Streptococcus mutans gene encoding **glucan binding protein B** and analysis of genetic diversity and protein production in clinical isolates.
AU Mattos-Graner, Renata O.; Jin, Song; King, William F.; Chen, Tsute; Smith, Daniel J.; Duncan, Margaret J. [Reprint author]
CS Department of Molecular Genetics, Forsyth Institute, 140 Fenway, Boston, MA, 02115, USA
mduncan@forsyth.org
SO Infection and Immunity, (November, 2001) Vol. 69, No. 11, pp. 6931-6941. print.
CODEN: INFIBR. ISSN: 0019-9567.

DT Article
LA English
ED Entered STN: 21 Nov 2001
Last Updated on STN: 25 Feb 2002
AB Streptococcus mutans, the primary etiological agent of dental caries, produces several activities that promote its accumulation within the dental biofilm. These include **glucosyltransferases**, their **glucan** products, and proteins that bind **glucan**. At least three **glucan** binding proteins have been identified, and **GbpB**, the protein characterized in this study, appears to be novel. The **gbpB** gene was cloned and the predicted protein sequence contained several unusual features and shared extensive homology with a putative peptidoglycan hydrolase from group B streptococcus. Examination of **gbpB** genes from clinical isolates of S. mutans revealed that DNA polymorphisms, and hence amino acid changes, were limited to the central region of the gene, suggesting functional conservation within the amino and carboxy termini of the protein. The **GbpB** produced by clinical isolates and laboratory strains showed various distributions between cells and culture medium, and amounts of protein produced by individual strains correlated positively with their ability to grow as biofilms in an in vitro assay.

L8 ANSWER 18 OF 18 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 11
AN 2001:303013 BIOSIS
DN PREV200100303013
TI Passive transfer of immunoglobulin Y antibody to Streptococcus mutans **glucan binding protein B** can confer protection against experimental dental caries.
AU Smith, Daniel J. [Reprint author]; King, William F.; Godiska, Ronald
CS Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA, 02115, USA
dsmith@forsyth.org
SO Infection and Immunity, (May, 2001) Vol. 69, No. 5, pp. 3135-3142. print.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002
AB Active immunization with Streptococcus mutans **glucan binding protein B** (GBP-B) has been shown to induce protection against experimental dental caries. This protection presumably results from continuous secretion of salivary antibody to GBP-B, which inhibits accumulation of S. mutans within the oral biofilm. The purpose of this study was to explore the influence of short-term (9- or 24-day) passive oral administration of antibody to S. mutans GBP-B on the longer-term accumulation and cariogenicity of S. mutans in a rat model of dental caries. Preimmune chicken egg yolk immunoglobulin Y (IgY) or IgY antibody to S. mutans GBP-B was supplied in lower (experiment 1) and higher (experiment 2) concentrations in the diet and drinking water of rats for 9 (experiment 1) or 24 (experiment 2) days. During the first 3 days of IgY feeding, all animals were challenged with 5X106 streptomycin-resistant S. mutans strain SJ-r organisms. Rats remained infected with S. mutans for 78 days, during which rat molars were sampled for the accumulation of S. mutans SJ-r bacteria and total streptococci. Geometric mean levels of S. mutans SJ-r accumulation on molar surfaces were significantly lower in antibody-treated rats on days 16 and 78 of experiment 2 and were lower on all but the initial (day 5) swabbing occasions in both experiments. Relative to controls, the extent of molar dental caries measured on day 78 was also significantly decreased. The decrease in molar caries correlated with the amount and duration of antibody administration. This is the first demonstration that passive antibody to S. mutans GBP-B can have a protective effect against cariogenic S. mutans infection and disease. Furthermore, this decrease in infection and disease did not require continuous antibody administration for the duration of the infection period. This study also indicates that antibody to components putatively involved only in cellular aggregation can have a significant effect on the incorporation of mutans streptococci in dental biofilm.